

PATENT COOPERATION TREATY
PCT
INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

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Applicant's or agent's file reference SPG/P100404WO	FOR FURTHER ACTION	WIPO PCT See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA4T6)
International application No. PCT/GB 03/02624	International filing date (day/month/year) 19.06.2003	Priority date (day/month/year) 19.06.2002
International Patent Classification (IPC) or both national classification and IPC A61K49/06		
Applicant KEELE UNIVERSITY et al.		

<ol style="list-style-type: none"> 1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36. 2. This REPORT consists of a total of 6 sheets, including this cover sheet. <ul style="list-style-type: none"> <input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT). <p>These annexes consist of a total of sheets.</p> 3. This report contains indications relating to the following items: <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the opinion II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input type="checkbox"/> Certain observations on the international application

Date of submission of the demand 16.01.2004	Date of completion of this report 21.09.2004
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Ansaldo, M Telephone No. +49 89 2399-7876



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB 03/02624

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-19 as originally filed

Claims, Numbers

1-153 as originally filed

Drawings, Sheets

1/4-4/4 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:
- the drawings, sheets:

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5. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).
(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

the entire international application,

claims Nos. 1-97,103-105,107-153

because:

the said international application, or the said claims Nos. 1-72,153 with respect to I.A. relate to the following subject matter which does not require an international preliminary examination (specify):
see separate sheet

the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-25,31-33,35-97,103-105,107-153 are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet

the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

the written form has not been furnished or does not comply with the Standard.

the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	23-24,49-69,95-96,124-144,146-148
	No: Claims	1-22, 25-48,70-94, 97-123, 145, 149-153
Inventive step (IS)	Yes: Claims	
	No: Claims	1-153
Industrial applicability (IA)	Yes: Claims	73-152
	No: Claims	

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2. Citations and explanations

see separate sheet

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Re Item III

Claims 1-72, 153 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

The Applicant is aware that the search report has been carried out for those parts of the application which are clear and supported within the meaning of Art.6 PCT and disclosed within the meaning of Art.5 PCT.

The examining division agrees with the objections put forward by the search division as to the partial search report under Art 6 PCTUnder Rule 66.1 (e) EPC, a preliminary examination is not carried out on matter which has not been searched.

Consequently, the preliminary examination has been carried out as if the compounds expressly mentioned in claims 26-30 and examples had been included in all independent claims.

Furthermore the preliminary examination has been also carried out on the parts of claims that have been searched, namely those parts relating to the manipulation of ion channels and to concrete diseases, specifically disclosed in the claims and examples.

Re Item V

1. D1 and D2 disclose the use of ferromagnetic particles (CrO_2) coated with RGD for magnetically manipulating a cell, such as an osteoblast. D1 reports that upregulation of Ca^{2+} influx into cells and induction of matrix mineralization has been achieved by applying a mechanical stress to the cells (p.93, first paragraph; p.95, 4.paragraph). D1 and D2 anticipate hereby the subject-matter of claims 1-22, 25-26,29-45, 70-94, 97-98,101-106, 110-120, 149-153 (Art. 33 (1) and (2)PCT).
2. D3 discloses that magnetic fields applied to collagen-coated ferric oxide beads (Fe_3O_4) induce stretch-activated Ca^{2+} flux in fibroblasts. D3 anticipates hereby the subject-matter of claims 1-22, 25-28,31-44, 70-94, 97-100,103-120, 149-153 (Art. 33 (1) and (2) CT).
3. D4 discloses the use of biocompatible magnetic nano- and microparticles to stimulate the growth of connective tissue by applying forces directly to the cell membrane and activating mechanosensitive transmembrane ion channels. D4 anticipates hereby the subject-matter of claims 1-21, 25,36-38, 70-93, 97,111-113, 149-153 (Art. 33 (1) and (2)PCT).

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4. D5 discloses the use of ferromagnetic particles (iron oxides) coated with antibodies or protein binding motifs, such as RGD, for magnetically manipulating cells, for altering production of molecules by the cells, mechanically disrupt membrane continuity and thereby permit delivery of large molecules, for targeting active compounds. D5 clearly states that the method can be used in living patients (p.4-p.5, I.19;p.9, I.30-p.11, I.27; p.12, I.5-10; p.17,I.30-38; p.27, I.12-21;claims). Therefore D5 anticipates the subject-matter of claims 3-5, 10-16, 26-28, 31-48, 70-77, 82-88, 99-100, 103-106, 109, 110-123, 145, 149-153 (Art. 33 (1) and (2) EPC).
5. Even by overcoming the above-mentioned novelty objections (Art. 33 (1) PCT) for claims 1-22, 25-48,70-94, 97-123, 145, 149-153 with the introduction of new embodiments, no inventiveness (Art. 33 (3) PCT) will be acknowledged, as the solution to the problem posed by the present application, namely the use of magnetisable particles for the manipulation of cells, in particular ion channels within the cell, has been already anticipated by the cited prior art.
6. Furthermore the present application only provides examples of manipulation of calcium channels *ex vivo*. The present application however does not provide any evidence of therapeutic effects *in vivo* at all.
Therefore, unless the applicant is able to provide credible and substantiated clinical data showing the efficacy of magnetisable particles for the treatment of the diseases mentioned in claims and their effect when combined with an active agent, demonstrating hereby that the problem posed has been solved, the presence of an **inventive step for claims 23-24,49-69,95-96,124-144,146-148**,as required by Article 33 (3) PCT, **will not be appreciated**.
- Examples which demonstrate the claimed effects may be submitted. These cannot be included in the application, as this would infringe Articles 19 (2) and 34 (2)(b). They will however remain in the file.
7. The potential relevant document WO 02 051985A (filing date 19.12.2001, priority date 23.12.2000, publication date 04.07.2002) is quoted according to Rules 70.10 and 64.3 PCT.